REMARKS

Applicants respectfully request reconsideration of the present application.

CLAIMS

Applicants have canceled claim 2 and 8, without prejudice or disclaimer. Applicants reserve the right to file one or more continuing applications directed to the canceled subject matter.

Applicants have amended claims 1 and 7, without prejudice or disclaimer. Applicants reserve the right to file one or more continuing applications directed to the subject matter omitted by the present amendment. Amended claims 1 and 7 represent the subject matter of claims 2 and 8, respectively, rewritten in an independent form. No new matter has been added.

The PTO should enter the present amendment because it cancels claims and presents the rejected claims in a better form for an appeal.

After the amendment, claims 1, 3-7 and 9-10 are pending. Applicants attached Appendix A, which displays the claim amendments according to regular prosecution practice.

FEBRUARY 11th and FEBRUARY 26th INTERVIEWS

Applicants thank Examiners Loewe and Shameem for the interviews.

During the February 11th interview, Applicants' representative discussed with Examiner Loewe the reissue oath/declaration objection. In the Interview Summary dated February 19, 2009, the PTO agreed to withdraw the objection.

During the February 26th interview, Applicants' representative discussed with Examiners Loewe and Shameem the enablement rejection; the obviousness rejection and the double patenting rejection. The subject matter of this interview may be gleaned from this response.

OATH/DECLARATION

In the January 12th Office Action, the PTO maintained the reissue oath/declaration objection. During the February 11th interview, Applicants' representative discussed with Examiner Loewe the reissue oath/declaration objection. In the Interview Summary dated February 19, 2009, the PTO agreed to withdraw the objection.

CLAIM REJECTIONS UNDER 35 U.S.C. §112, ¶ 1

Claims 1, 2 and 7-10 stand rejected because the specification, while being enabling for the method of treating hypertension, does not provide enablement for the method of treating the broader scope of "angiotensin II-mediated diseases". Applicants respectfully traverse.

Applicants addressed the rejection on pages 4-6 of their response filed September 10, 2008. On page 3 of the January 12th Office Action, the PTO indicated that Applicants' remarks are not persuasive. The PTO explained its position as follows: "The cited art shows the level of unpredictability in Applicant's field of endeavor, i.e. treatment of myocardial infarction using angiotensin II antagonists."

Applicants respectfully submit that the PTO ignored the evidence and the sound scientific reasoning that Applicants provided with their September 10th response.

THE PTO MUST WEIGH ALL THE EVIDENCE

Applicants respectfully submit that, according to MPEP § 2164.05:

> "The examiner must then *weigh all the evidence* before him or her, including the specification and any new evidence supplied by applicant with the evidence and/or sound scientific reasoning previously presented in the rejection and decide whether the claimed invention is enabled. *The examiner should never make the determination based on personal opinion*. The determination should always be based on the *weight of all the evidence.*" (Emphasis added)

Applicants respectfully urge the PTO to consider all the evidence including Demers et al. JAMA, 2005, 294(14), 1794-1798, and Drs. Tsuyuki and McDonald's statement on page 854 of Strauss and Hall, Circulation 2006; 144; 838-854.

For the PTO's convenience, Applicants reiterate the major points of their September 10th argument.

The PTO bases its rejection largely on the thesis that "angiotensin II receptor antagonists *may increase the risk of myocardial infarction*", see page 4 of the March 25th Office Action, which the PTO supports by the article on Strauss and Hall, Circulation 2006; 144; 838-854. Strauss and Hall call a phenomenon of the increased risk of myocardial infarction caused by angiotensin II receptor an ARB-MI paradox.

1) ARB-MI paradox was introduced for valsartan, which is not the claimed angiotensin II antagonist

Applicants submit that the ARB-MI paradox was introduced in a paper coauthored by Strauss (Verma and Strauss, BMJ, 2004, 329, 1248-1249), based on the data from the VALUE trial, which showed a relative increase in MI for one particular angiotensin II antagonist, valsartan, see Strauss, page 839. Applicants respectfully point out that valsartan is an angiotensin II antagonist, which is different from the angiotensin II antagonists recited in the present claims.

2) Strauss disregards data for the claimed angiotensin II antagonists because they do not support his "paradox" theory

In his CIRCULATION paper, which was cited by the PTO, Strauss tries to fit the data from clinical trials for other angiotensin II antagonists into his "paradox" theory. In doing so, Strauss tends to disregard the data that do not support his paradox. For example, Strauss disregards the data from the CHARM (Candesartan in Heart Failure: Assessment of Reduction in Mortality and Morbidity) program in making his conclusions, although he explicitly admits the following results of the CHARM: "Candesartan reduced all-cause mortality (hazard ratio 0.91, 95 % confidence interval [CI] 0.83 to 1.0, P=0.055)" see page 844, left column; "a reanalysis of CHARM suggests candersartan reduces the composite outcome of CV death or non fatal MI", see page 844, left column; "there was a reported nonsignificant reduction in MI (candesartan 57 versus placebo 73; P=0.15), see page 846, right column.

3) The claimed antiotensin II antagonist, candesartan significantly reduces the risk of the composite outcome of cardiovascular death or nonfatal MI

Applicants respectfully submit that to access the effect of the claimed angiotensin II antagonists on myocardial infarction, one or ordinary skill in the art would not have relied on Strauss and his controversial "paradox" theory. Instead, one of ordinary skill in the art would look at the results of the CHARM program in the paper by Demers et al. JAMA, 2005, 294(14), 1794-1798, which demonstrate that "candesartan significantly reduces the risk of the composite outcome of cardiovascular death or nonfatal MI", see Conclusion, page 1794.

4) ARB-MI paradox was not accepted by those of ordinary skill in the art

Applicants further submit that the thesis, upon which the PTO relies to support its position, is highly controversial and is not widely supported and accepted by those of ordinary skill in the art. For example, the very same article by Strauss and Hall that the PTO uses to support the thesis contains on page 854 "Response to Strauss and Hall", in which Drs. Tsuyuki and McDonald state "Our basic thesis was simple: ARBs do not increase risk of MI" (ARB is angiotensin II receptor blocker, MI is miocardical infarction). In the last sentence of their "Response to Strauss and Hall", Drs. Tsuyuki and McDonald conclude that "although Drs Strauss and Hall have coined the phrase "the ARB paradox," we are left wondering where the paradox is" referring to the ARB-MI paradox defined on page 839 of Strauss.

Summary

In sum, the PTO's rejection relies on a controversial theory, which ignores real experimental results demonstrating the reduction of the risk of MI by the claimed angiotensin II antagonists. For this reason alone, Applicants request withdrawal of the rejection.

CLAIM REJECTION UNDER 35 U.S.C. §103

Claims 1-10 stand rejected as obvious over Naka (EP 0520423 and EP 0459136) in view of Weinstock (WO/10097) further in view of Wong (caplus AN 91307690, American Journal of Hypertension, vol. 4, 288S-298S, 1991). Applicants respectfully traverse.

I) SUMMARY OF APPLICANTS' SEPTEMBER 10TH RESPONSE

Applicants addressed the rejection on pages 6-10 of their response filed September 10, 2009. The major points in the Applicants' traversal of the rejection were as follows:

1) The PTO failed to establish a prima facie case of obviousness because the PTO failed to make its obviousness analysis explicit.

In *KSR International Co. v. Teleflex Inc.*, 550 U.S._, 82 USPQ2d 1385 (2007), the Supreme Court emphasized that the analysis supporting a rejection under 35 U.S.C. §103(a) should be made explicit. The Supreme Court also stated, quoting *In re Kahn*, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006), that "'[R]ejections on obviousness cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning the legal conclusion of obviousness.'"

Applicants respectfully submitted that at least two statements in the PTO's formulation of the rejection are conclusory.

In particular, Applicants pointed out that to make a rejection proper, the PTO is required to provide "some articulated reasoning with some rational underpinning" to support a substitution Weinstock's angiotensin II antagonist with Naka's angiotensin II antagonists in Weinstock's combinations.

2) The claimed subject matter demonstrates unexpected results

In particular, Applicants referred the PTO to a) Kim *et al.*, *Hypertension*, vol. 35 (2000) 769-774, which Applicants submitted previously with their response filed May 31, 2005 and which demonstrates unexpected results for candesartan cilexetil and amlodipine and b) Demers et al. JAMA, 2005, 294(14), 1794-1798, which demonstrates unexpected results for candesartan and diuretic.

3) The PTO allowed composition claims identical in scope to claims 1-3.

Applicants respectfully submitted, with respect to claims 1-3, that the PTO allowed composition claims of identical scope in the parent application, now U.S. Pat. No. 6,228,874.

Because the PTO granted these claims, Applicants respectfully submit that no reason exists why the present method claims should not also be allowable.

II) THE PTO'S COMMENTS ON APPLICANTS' SEPTEMBER 10th RESPONSE

In the January 12th Office Action, the PTO indicated that Applicants' September 10th traversal of the rejection is unpersuasive. In support of its position, the PTO provided the following commentary on page 3 of the January 12th Office Action:

> "Notwithstanding lack of explicit suggestion to combine the instantly claimed compound with diuretic and/or calcium channel blocker, the combination is still found to obvious for the reasons provided in the previous office action. Notably, the instant compound is an angiotensin II antagonist which art recognized to be useful in combination with the other ingredients for the instant utility. The combination is within the technical grasp of one of ordinary skill, at the time the application was filed."

The PTO also supported its position by referring to so-called "obvious to try" rationale from MPEP § 2143.

III) APPLICANTS' RESPONSE TO THE PTO'S COMMENTARY

1) The PTO did not consider points 2 and 3 in Applicants's September 10th non-obviousness argument

Applicants respectfully submit that the PTO's commentary addresses only point 1) presented in Applicants' September 10th response. Applicants submit that the PTO's commentary did not address points 2 and 3 of the September 10th response. Applicants urge the PTO to consider points 2) and 3) and provide an explanation why these separate Applicants' arguments are insufficient to overcome the rejection.

2) The PTO confuses "explicit analysis" and "explicit suggestion"

Based on the cited above excerpt from the January 12th Office Action, it appears that the PTO confuses "explicit analysis" and "explicit suggestion". Applicants respectfully submit that providing explicit analysis to an obviousness rejection means providing "some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness", see *In re Kahn* citation *supra*.

3) A mere citation of the "obvious to try" rationale from MPEP does not exempt the PTO from making its obviousness analysis explicit

Applicants submit that a mere citation of guidelines for the "obvious to try" rationale from MPEP § 2143 does not exempt the PTO from making its obviousness analysis.

Applicants respectfully submit that the cited in the January 12th Office Action guidelines from MPEP § 2143 specify four requirements that PTO **must** satisfy in order to make its obviousness analysis explicit and thereby establish a *prima facie* case of obviousness based on the "obvious to try" rationale.

"Office personnel **must articulate** the following:

(1) a finding that at the time of the invention, there had been a recognized problem or need in the art, which may include a design need or market pressure to solve a problem;

(2) a finding that there had been a **finite number of** identified, **predictable** potential solutions to the recognized need or problem;

(3) a finding that one of ordinary skill in the art could have pursued the known potential solutions with a reasonable expectation of success; and

(4) whatever additional findings based on the *Graham* factual inquiries may be necessary, in view of the facts of the case under consideration, to explain a conclusion of obviousness." (Emphasis added)

"If **any of these findings cannot be made, then this rationale cannot be used** to support a conclusion that the claim would have been obvious to one of ordinary skill in the art." (Emphasis added)

Since the PTO did not articulate any of the four required findings, the PTO cannot rely on the "obvious to try" rationale.

DOUBLE PATENTING REJECTIONS

The PTO has maintained five multiple-reference double-patenting rejections, which cite one of U.S. patents nos. 5,736,555; 5,583,141; 5,243,054; 7,294,344 and 6,589,547, as a primary reference, in combination with Weinstock et al. (WO 92/10097) further in view of Wong et al. (caplus AN 91307690, American Journal of Hypertension, vol. 4, 288S-298S, 1991).

Applicants addressed each of the rejections on pages 10-14 of the response filed September 10, 2008. In the January 12th Office Action, the PTO maintained all five multiple-reference double-patenting rejections. Applicants respectfully submit that, in the January 12 Office Action, the PTO did not provide any justification for maintaining the rejections as the PTO combined its comments for the double patenting and the obviousness rejections. Applicants respectfully urge the PTO to consider Applicants' comments regarding the double patenting rejections in the September 10th response.

Although Applicants disagree with each of the five multiple reference rejections, to advance the prosecution only, Applicants submit with the present response a terminal disclaimer over U.S. patents nos. 7,294,344 and 6,589,547

Prior to addressing each of the multiple reference double patenting rejections based on U.S. patents nos. 5,736,555; 5,583,141 and 5,243,054 as a primary reference, Applicants provide the following commentary, which should be considered together with Applicants' commentary in the September 10th response:

1) The PTO relies on non-claimed disclosure 5,736,555 and 5,583,141

Applicants respectfully submit that, in the double patenting rejections citing 5,736,555 and 5,583,141 as a primary reference, the PTO relies on a non-claimed disclosure in these patents, which is inappropriate in double patenting rejections. Applicants respectfully refer the PTO to MPEP §804.III, which explains the difference between double patenting rejections and 35 U.S.C. 103(a) as follows:

> "One significant difference is that a **double patenting rejection must rely on a comparison with the claims** in an issued or to be issued patent, whereas an >anticipation or< obviousness rejection based on the same patent under 35 U.S.C. 102(e)/ 103(a) relies on a comparison with what is disclosed (whether or not claimed) in the same issued or to be issued patent. In a 35 U.S.C. 102(e)/103(a) rejection over a prior art patent, the reference patent is available for all that it fairly discloses to one of ordinary skill in the art, regardless of what is claimed. *In re Bowers*, 359 F.2d 886, 149 USPQ 570 (CCPA 1966)."
>
> Also, see MPEP §804.II,

"A double patenting rejection of the obviousness-type>, if not based on an anticipation rationale,< is "analogous to [a failure to meet] the nonobviousness requirement of 35 U.S.C. 103" **except that the patent principally underlying the double patenting rejection is not considered prior art**. *In re Braithwaite*, 379 F.2d 594, 154 USPQ 29 (CCPA 1967)." (Emphasis added)

"When considering whether the invention defined in a claim of an application would have been an obvious variation of the invention defined in the claim of a patent, **the disclosure of the patent may not be used as prior art**. *General Foods Corp. v. Studiengesellschaft Kohle mbH*, 972 F.2d 1272, 1279, 23 USPQ2d 1839, 1846 (Fed. Cir. 1992)." (Emphasis added)

2) The PTO does not provide clear reasons why ordinary artisan would conclude that the claimed inventions are obvious variations of the invention defined in a claim of the patent.

Applicants respectfully submit that MPEP §804.II provides the following guidelines for obviousness-type double patenting rejections:

"Any obviousness-type double patenting rejection **should make clear**:

(A) The differences between the inventions defined by the conflicting claims - a claim in the patent compared to a claim in the application; and

(B) The reasons why a person of ordinary skill in the art would conclude that the invention defined in the claim at issue >is anticipated by, or< would have been an obvious variation of >,< the invention defined in a claim in the patent." (Emphasis added)

Applicants respectfully submit that for each of the multiple-reference double patenting rejections, the PTO addresses only point A), i.e. the PTO does not provide **clear** reasons why one ordinary skill in the art would conclude that the claimed inventions are obvious variations of the invention defined in a claim of the patent cited as a primary reference.

Applicants submit, for each of the multiple reference double patenting rejections based on U.S. patents nos. 5,736,555 and 5,583,141, the PTO admits that claims of these patents do not recite the claimed angiotensin II compounds. Furthermore, for each of the double patenting rejections based on U.S. patents nos. 5,736,555, 5,583,141 and 5,243,054, the PTO admits that claims of these patents do not recite the claimed combinations, which include a compound having a diuretic activity or a compound having calcium antagonistic activity.

Applicants respectfully submit that the PTO does **not** provide clear reasons why one of ordinary skill in the art would find the claimed angiotensin II compounds obvious variations of claims of U.S. patents nos. 5,736,555 and 5,583,141. Furthermore, the PTO does **not** provide clear reasons why one of ordinary skill in the art would conclude that the claimed combinations, which include a compound having a diuretic activity or a compound having calcium antagonistic activity, are obvious variations of claims of U.S. patents nos. 5,736,555, 5,583,141 and 5,243,054.

3) The PTO's logic in the multiple reference double patenting rejections precludes any claim directed to a combination from being patentable over claims of a patent claiming an element of the combination

Applicants respectfully further submit that the logic, on which the PTO relies combining one of U.S. patents nos. 5,736,555, 5,583,141 and 5,243,054 with Weinstock and Wong in its multiple reference double patenting rejections, would make any claim directed to a combination A+B rejected over a patent claiming A on the ground of non-statutory obviousness-type double patenting if a) there is a separate **non-claimed** disclosure of a combination C+B and b) A and C can act by the same mechanism.

Claims 1-10 stand rejected on the ground of non-statutory obviousness-type double patenting as unpatentable over claims 1-6, 8-12, 14-16, 19, 20 and 23-25 of U.S. Patent No. 5,736,555 in view of Weinstock et al. (WO 92/10097) further in view of Wong et al. (caplus AN 91307690, American Journal of Hypertension, vol. 4, 288S-298S, 1991). Applicants respectfully traverse.

As admitted by the PTO on page 10 of the Office Action dated March 25, 2008, the claims of the '555 patent do not recite the particular angiotensin II antagonists of the instant claims. Furthermore, as admitted by the PTO on page 10 of the March 25th Office Action, the claims the '555 patent do not recite a combination of angiotensin II antagonist with a calcium channel blocker and/or a diuretic.

To remedy the admitted deficiencies of the '555 patent, the PTO relies on the **non-claimed** disclosure of the '555 patent to arrive at the particular angiotensin II antagonists

recited in the instant claims. Furthermore, to arrive at the combinations of angiotensin II antagonist with a calcium channel blocker or a diuretic recited in the instant claims, the PTO relies on Weinstock and Wong.

As explained in the Applicants commentary above and the Applicants commentary on pages 10-14 of the September 10th response, the deficiencies of the PTO's position are as follows:

1) The PTO relies on the **non-claimed** disclosure the 555 patent for the double patenting rejections.

2) The PTO does not provide clear reasons why ordinary artisan would conclude that the claimed inventions are obvious variations of the invention defined in claims of the '555 patent.

In particular, the PTO does **not** provide clear reasons why one of ordinary skill in the art would find the angiotensin II compounds recited in the instant claims obvious variations over claims of the '555 patent, without relying on the **non-claimed** disclosure the '555 patent.

Furthermore, the PTO does **not** provide clear reasons why one of ordinary skill in the art would conclude that the claimed combinations, which include a compound having a diuretic activity or a compound having calcium antagonistic activity, are obvious variations of claims of the '555 patent. As Applicants explained above, the PTO's logic, on which the PTO relies combining the claims of the '555 patent with Weinstock and Wong, would make any claim directed to a combination A+B rejected over a patent claiming A on the ground of non-statutory obviousness-type double patenting if a) there is a separate **non-claimed** disclosure of a combination C+B and b) A and C can act by the same mechanism.

3) The PTO ignores the expected results of the claimed combinations as evidenced by Kim *et al.*, *Hypertension*, vol. 35 (2000) 769-774 and Demers et al. JAMA, 2005, 294(14), 1794-1798, see Applicants' September 10th response.

In sum, at least for these reasons, the claims are patentable over the claims of the '555 patent, Weinstock and Wong. Accordingly, Applicants respectfully request the PTO to reconsider and withdraw the rejection.

Claims 1-10 stand rejected on the ground of non-statutory obviousness-type double patenting as unpatentable over claims 1-6, 8-16, 19, 20 and 23-25 of U.S. Patent no. 5,583,141 in view of Weinstock et al. (WO 92/10097) further in view of Wong et al. (caplus AN 91307690, American Journal of Hypertension, vol. 4, 288S-298S, 1991). Applicants respectfully traverse.

As admitted by the PTO on page 11 of the March 25th Office Action, the claims of the '141 patent do not recite the particular angiotensin II antagonists of the instant claims. Furthermore, as admitted by the PTO on page 11 of the March 25th Office Action, the claims the '141 patent do not recite a combination of angiotensin II antagonist with a calcium channel blocker and/or a diuretic.

To remedy the admitted deficiencies of the '141 patent, the PTO relies on the **non-claimed** disclosure of the '141 patent to arrive at the particular angiotensin II antagonists recited in the instant claims. Furthermore, to arrive at the combinations of angiotensin II antagonist with a calcium channel blocker or a diuretic recited in the instant claims, the PTO relies on Weinstock and Wong.

As explained in the Applicants commentary above and the Applicants commentary on pages 10-14 of the September 10th response, the deficiencies of the PTO's position are as follows:

1) The PTO relies on the **non-claimed** disclosure the '141 patent for the double patenting rejections.

2) The PTO does not provide clear reasons why ordinary artisan would conclude that the claimed inventions are obvious variations of the invention defined in claims of the '141 patent.

In particular, the PTO does **not** provide clear reasons why one of ordinary skill in the art would find the angiotensin II compounds recited in the instant claims obvious variations over claims of the '141 patent, without relying on the **non-claimed** disclosure the '141 patent.

Furthermore, the PTO does **not** provide clear reasons why one of ordinary skill in the art would conclude that the claimed combinations, which include a compound having a diuretic activity or a compound having calcium antagonistic activity, are obvious variations of claims of the '141 patent. As Applicants explained above, the PTO's logic, on which the PTO relies combining the claims of the '141 patent with Weinstock and Wong, would make any claim directed to a combination A+B rejected over a patent claiming A on the ground of non-statutory obviousness-type double patenting if a) there is a separate **non-claimed** disclosure of a combination C+B and b) A and C can act by the same mechanism.

3) The PTO ignores the expected results of the claimed combinations as evidenced by Kim *et al.*, *Hypertension*, vol. 35 (2000) 769-774 and Demers et al. JAMA, 2005, 294(14), 1794-1798, see Applicants' September 10th response.

In sum, at least for these reasons, the present claims are patentable over the claims of the '141 patent, Weinstock and Wong. Accordingly, Applicants respectfully request the PTO to reconsider and withdraw the rejection.

Claims 1-10 stand rejected on the ground of non-statutory obviousness-type double patenting as unpatentable over claim 1 of U.S. Patent no. 5,243,054 in view of Weinstock et al. (WO 92/10097) further in view of Wong et al. (caplus AN 91307690, American Journal of Hypertension, vol. 4, 288S-298S, 1991). Applicants respectfully traverse.

As admitted by the PTO on page 12 of the March 25th Office Action, the claim the '054 patent do not recite a combination of angiotensin II antagonist with a calcium channel blocker and/or a diuretic.

To remedy the admitted deficiencies of the claim of the '054 patent, the PTO relies on Weinstock and Wong.

As explained in the Applicants commentary above and the Applicants commentary on pages 10-14 of the September 10th response, the deficiencies of the PTO's position are as follows:

1) The PTO does not provide clear reasons why ordinary artisan would conclude that the claimed inventions are obvious variations of the invention defined in claims of the '054 patent.

In particular, the PTO does **not** provide clear reasons why one of ordinary skill in the art would conclude that the claimed combinations, which include a compound having a diuretic activity or a compound having calcium antagonistic activity, are obvious variations of claims of the '054 patent. As Applicants explained above, the PTO's logic, on which the PTO relies combining the claims of the '054 patent with Weinstock and Wong, would make any claim directed to a combination A+B rejected over a patent claiming A on the ground of non-statutory obviousness-type double patenting if a) there is a separate **non-claimed** disclosure of a combination C+B and b) A and C can act by the same mechanism.

2) The PTO ignores the expected results of the claimed combinations as evidenced by Kim *et al.*, *Hypertension*, vol. 35 (2000) 769-774 and Demers et al. JAMA, 2005, 294(14), 1794-1798, see Applicants' September 10th response.

In sum, at least for these reasons, the claims are patentable over the claim of the '054 patent, Weinstock and Wong. Accordingly, Applicants respectfully request the PTO to reconsider and withdraw the rejection.

Claims 1-10 stand rejected on the ground of non-statutory obviousness-type double patenting as unpatentable over claims 1-15 and 17 of U.S. Patent no. 7,294,344 in view of Weinstock et al. (WO 92/10097) further in view of Wong et al. (caplus AN 91307690, American Journal of Hypertension, vol. 4, 288S-298S, 1991).

Although Applicants disagree with the PTO's rejection, to advance the prosecution only, Applicants submit herewith a terminal disclaimer over U.S. Patent no. 7,294,344. In view of the terminal disclaimer, Applicants respectfully request withdrawal of the rejection.

Claims 1-10 stand rejected on the ground of non-statutory obviousness-type double patenting as unpatentable over claims 1-15 and 17 of U.S. Patent no. 6,589,547 in view of Weinstock et al. (WO 92/10097) further in view of Wong et al. (caplus AN 91307690, American Journal of Hypertension, vol. 4, 288S-298S, 1991). Applicants respectfully traverse.

Although Applicants disagree with the PTO's rejection, to advance the prosecution only, Applicants submit herewith a terminal disclaimer over U.S. Patent no. 6,589,547. In view of the terminal disclaimer, Applicants respectfully request withdrawal of the rejection.

CONCLUSION

Applicants believe that the present application is in condition for allowance. Favorable reconsideration of the application is respectfully requested. The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing or a credit card payment form being unsigned, providing incorrect information resulting in a rejected credit card transaction, or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,
Alexey Saprigin

Date March 16, 2009

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APPENDIX A

1. (Currently Amended) A method for the treatment of angiotension II-mediated disease in a mammal in need thereof which comprises administering an effective amount of (±)-1-(cyclohexyloxycarbonyloxy)ethyl 2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)biphenyl-4-yl]methyl]-1H-benzimidazole-7-carboxylate,
2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)biphenyl-4-yl]methyl]-1H-benzimidazole-7-carboxylic acid, or
2-ethoxy-1-[[2'-(2,5-dihydro-5-oxo-1,2,4-oxadiazol-3-yl)biphenyl-4-yl]methyl]-1H-benzimidazole-7-carboxylic acid, or a pharmaceutically acceptable salt thereof, in combination with an effective amount of furosemide**, wherein the disease is hypertension, cardiac insufficiency, ischemic peripheral circulation disturbances, myocardial ischemia, vein insufficiency, progressive cardiac insufficiency after myocardial infarction, diabetic nephritides, nephritis, arteriosclerosis, hyperaldosteronism, dermatosclerosis, glomerulosclerosis, renal insufficiency, diseases of central nervous system, sensory disturbances, deficiency of memory, depression, amnesia and senile dementia, anxiety neurosis, catatonia, glaucoma, or intraocular high tension**.

2. (Canceled)

3. (Patented) A method according to claim 1, wherein the disease is hypertension.

4. (Previously Presented) A pharmaceutical composition which comprises at least one of :
(±)-1-(cyclohexyloxycarbonyloxy)ethyl 2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)biphenyl-4-yl]methyl]-1H-benzimidazole-7-carboxylate,
2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)biphenyl-4-yl]methyl]-1H-benzimidazole-7- carboxylic acid, or
2-ethoxy-1-[[2'-(2,5-dihydro-5-oxo-1,2,4-oxadiazol-3-yl)biphenyl-4-yl]methyl]-1H-benzimidazole-7-carboxylic acid, or a pharmaceutically acceptable salt thereof, in combination with a compound having diuretic activity or a compound having calcium antagonistic activity.

5. (Previously Presented) The composition of claim 4, in which the compound having diuretic activity is a member selected from the group consisting of amiloride, chlorothiazide, benzthiazide, ticrynafen, acetazolamide, aminophylline, cyclothiazide, cyclopenthiazide, methyclothiazide, benzylhydrochlorothiazide, penfluthiazide, ethiazide, hydroflumethiazide, polythiazide, clofenamide, chlorthalidone, cyclothiazide, bendroflumethiazide, meticrane, tripamide, metolazone, quinethazone, bumetanide, mefruside, azosemide, ethacrynic acid, sodium ethacrynate, piretanide, spironolactone, potassium canrenoate and triamterene.

6. (Previously Presented) The composition of claim 4, in which the compound having calcium antagonistic activity is a member selected from the group consisting of diltiazem hydrochloride, terolidine hydrochloride, nicardipine hydrochloride, barnidipine hydrochloride, flunarizine hydrochloride, verapamil hydrochloride, cinnarizine, nisoldipine, nitrendipine, nifedipine, nilvadipine, felodipine, nildipine, nimodipine, penidipine and benidipine.

7. A method for treatment of **an** angiotensin II mediated **disease** ~~diseases~~ in a mammal in need thereof which comprises administering an effective amount of at least one of (±)-1-(cyclohexyloxycarbonyloxy)ethyl 2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)biphenyl-4-yl]methyl]-1H-benzimidazole-7-carboxylate,
2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)biphenyl-4-yl]methyl]-1H-benzimidazole-7- carboxylic acid, or
2-ethoxy-1-[[2'-(2,5-dihydro-5-oxo-1,2,4-oxadiazol-3-yl)biphenyl-4-yl]methyl]-1H-benzimidazole-7-carboxylic acid, or a pharmaceutically acceptable salt thereof, in combination with a compound having diuretic activity or a compound having calcium antagonistic activity, **wherein the angiotensin II-mediated disease is selected from the group consisting of hypertension, cardiac insufficiency, ischemic peripheral circulation disturbances, myocardial ischemia, vein insufficiency, progressive cardiac insufficiency after myocardial infarction, diabetic nephritides, nephritis, arteriosclerosis, hyperaldosteronism, dermatosclerosis, glomerulosclerosis, renal insufficiency, diseases of central nervous system, sensory disturbances, deficiency of memory, depression,**

amnesia and senile dementia, anxiety neurosis, catatonia, glaucoma and intraocular high tension.

8. (Canceled)

9. (Previously Presented) The method of claim 7, wherein the compound having diuretic activity is a member selected from the group consisting of amiloride, chlorothiazide, benzthiazide, ticrynafen, acetazolamide, aminophylline, cyclothiazide, trichloromethiazide, cyclopenthiazide, hydrochlorothiazide, methyclothiazide, benzylhydrochlorothiazide, penfluthiazide, ethiazide, hydroflumethiazide, polythiazide, clofenamide, chlorthalidone, cyclothiazide, bendroflumethiazide, meticrane, tripamide, metolazone, indapamide, quinethazone, furosemide, bumetanide, mefruside, azosemide, ethacrynic acid, sodium ethacrynate, piretanide, spironolactone, potassium canrenoate and triamterene.

10. (Previously Presented) The method of claim 7, wherein the compound having calcium antagonistic activity is a member selected from the group consisting of diltiazem hydrochloride, terolidine hydrochloride, nicardipine hydrochloride, barnidipine hydrochloride, flunarizine hydrochloride, verapamil hydrochloride, manidipine hydrochloride, cinnarizine, nisoldipine, nitrendipine, nifedipine, nilvadipine, felodipine, nildipine, nimodipine, penidipine and benidipine.